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EXAMINER	
ARCHIE, NINA	

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1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/049,967	DOLLY ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *29 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48,50,53-55,57-60,62,69,70,73 and 75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48,50,53-55,57-60,62,69,70,73 and 75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 6-29-07. Claims 48, 50, 53-55, 57-60, 62, 69, 70, 73 and 75 are pending. Claims 48, 50, 57, 58 and 75 have been amended. Claim 61 has been cancelled.

Objections/Rejections Withdrawn

2. In view of the Applicant's amendment and remark following objections are withdrawn.

a) Objection to claim 75, page 2 last 3 line and page 3 first 3 lines is withdrawn in light of applicant's amendment thereto.

b) Rejection of claim 75 under 35 U.S.C. 112, first paragraph, page 3 is withdrawn in light of applicant's amendment thereto.

c) Rejection of claims 48, 50, 53, 57-62 and 70 under 35 U.S.C. 102(b) as to reference Siegal et al, page 6 last paragraph and pages 7-8 is withdrawn in light of applicant's amendment thereto.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. The rejection of claims 48, 50, 53-55, 57-62, 69-70, 73, and 75 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description is maintained for the reasons set for in the previous office action.

Applicant arguments:

A) The Applicants submit that the specification teaches numerous structural limitations of SNAP-25 that result in a toxin-resistant SNAP-25 and/or toxin-inhibitory SNAP-25.

With respect to toxin-resistant SNAP-25s, the specification teaches that alterations of the P1 and/or PI' residues of a botulinum cleavage site in SNAP-25 produces a toxin-resistant SNAP-25. For example, the specification teaches that that alterations of the P1 and/or P'I positions of a botulinum cleavage site in SNAP-25 produces a toxin-resistant SNAP-25 and discloses at least 15 single-substitutions that produce a toxin-resistant SNAP-25 molecules and over 36 multiple substitutions that produce a toxin-resistant SNAP-25 molecules. See, e.g., pg. 13, line 25 through pg. 14, line 8; pg. 15, lines 14-29; pg. 22, line 14 through pg. 23, line 8; and Examples 1 and 2. As one instance, FIG. 3 of present specification teaches that changing the endogenous QR amino acids comprising the P1-P'I positions flanking the cleavage bond of botulinum toxin A to QT, QA, AA, AK, KH, or WW result in a toxin-resistant SNAP-25. As another instance, the present specification teaches that changing the R located at the P1 position flanking the cleavage bond of botulinum toxin C1 to A, S, T, D or E produces a toxin-resistant SNAP-25. As yet another instance, the present specification teaches that changing the I located at the P'I position flanking the cleavage bond of botulinum toxin E to F, G, S or N produces a toxin-resistant SNAP-25. Additionally, the present specification teaches that changing the RQIDRIM sequence comprising the cleavage site for botulinum toxin E to PQIKRIT results in a toxin-resistant SNAP-25. Lastly, based on the present specification, a person of ordinary skill in the art would reasonably expect that insertions, which disrupt the P1-P'I cleavage sites, would result in a toxin-resistant SNAP-25.

As another example, the specification also teaches that deletion of residues produces a toxin-resistant SNAP-25. As one instance, the present specification indicates that amino- terminal deletion of residues 202-206 of SNAP-25 creates a toxin-resistant SNAP-25. See, e.g., pg. 17, lines 19-26; and Examples 1 and 2. As another instance, the present specification indicates that amino-terminal deletion of residues 1-141 of SNAP-25 creates a toxin-resistant SNAP-25. See, e.g., pg. 20, lines 8-18; and

Examples 1 and 2. A person of ordinary skill in the art would reasonably expect that similar deletions, such as, e.g., deletion of amino acids 1-140, 1-139, 1-138, 1-137, 1-136, 1-135, 1-134, 1-133, 1-132, 1-131, 1-130, etc., would behave similarly the toxin-resistant SNAP-25 having amino acids 1-141 deleted. The present specification also discloses that combining the amino-terminal and carboxyl- terminal deletions will also produce toxin-resistant SNAP-25s. See, e.g., pg. 20, lines 8-18; and Examples 1 and 2. With respect to toxin-inhibitory SNAP-25, the specification teaches that alterations of the P1 and/or PI' residues of a botulinum cleavage site in SNAP-25 produces a toxin-inhibitory SNAP-25 and discloses many examples. See, e.g., pg. 18, line 21 through pg. 19, line 4; pg. 29, line 19 through pg. 30, line 28; pg. 37, lines 6-28; and Example 1. As such, the substitutions and insertions discussed above would also produce toxin-inhibitory SNAP-25s. In addition, the present specification indicates other alterations also produce a toxin- inhibitory SNAP-25. For instance, substituting the Q197 with C results in a toxin-inhibitory SNAP-25.

As another example, the specification also discloses many deletion-based alterations in SNAP-25 that produce a toxin-inhibitory SNAP-25. See, e.g., pg. 29, line 19 through pg. 30, line 28; pg. 35, lines 22-25; pg. 38, lines 5-12; and Examples 1 and 2. As one instance, the present specification indicates that amino-terminal deletion of residues 198-206 of SNAP-25 creates a toxin-inhibitory SNAP-25. See pg. 29, lines 27-29. As another instance, the present specification indicates that amino-terminal deletion of residues1-180 or 1-186 of SNAP-25 creates a toxin-inhibitory SNAP-25. See pg. 30, lines 18-28. A person of ordinary skill in the art would reasonably expect that similar deletions, such as, e.g., deletion of amino acids 1-181, 1-182, 1-183, 1-184, or 1-185, would behave similarly the toxin-inhibitory SNAP-25 having amino acids 1-180 or 1-186 deleted. The present specification also discloses that combining the amino-terminal and carboxyl-terminal deletions will also produce toxin-inhibitory SNAP-25s.

The specification further teaches how to generate and test for additional SNAP-25 variants useful as a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25. See, e.g., pg. 23, lines 23-27 disclosing exocytosis assays; pg. 33, lines 5-8 disclosing treatment effect assays; pg. 33, line 18 through pg. 34, line 28 disclosing peptide synthesis

techniques; pg. 38, lines 25- 29 disclosing mutagenesis techniques; pg. 38, line 14 through pg. 45, line 14 disclosing DNA cloning and protein expression techniques. In addition, Examples 1 and 2 of the present specification illustrate how to use these disclosed techniques to generate and test for SNAP-25 variants useful as a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25.

Examiner's Response to Applicant's Arguments:

B) The Examiner accepts that the specification teaches numerous examples of SNAP-25. However the specification does not teach structural limitations of SNAP-25. Applicant's arguments have been considered but are not found to be persuasive in view the fact that it is known in the art for nucleic acids as well as proteins, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effect of these changes are largely unpredictable as to which one have significant effect versus not. Therefore, the Applicants multitude of structural limitations taught in the specification distinguishing identifying characteristics of a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25, in the form of amino acid substitutions, deletions and insertions, also taught by the present specification results in an unpredictable and therefore unreliable correspondence of SNAP-25 and known function and therefore lacks support regarding utility and/or enablement. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as noting certain conserved sequences in limited specific cases: Gerhold et al [BioEssays, Vol.18, pages. 973-981 {1996}]. Therefore, the claim invention thus the claims do not meet the written description requirement the rejection is maintained.

Claim Rejections Maintained

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. The rejection of claims 48, 50, 53-55, 57-62 and 69-70 under 35 U.S.C. 102(b) as being anticipated by anticipated by Carroll et al US Patent No. 5,599,539 Date February 4, 1997 is maintained for the reason set forth in the previous office action.

Applicant arguments:

A) First, the Applicants respectfully disagree with the Examiner's interpretation of the meaning for the term "SNAP-25." As pointed out by the Examiner, a polypeptide variant includes insertions, deletions, conservative substitutions and/or non-conservative substitutions. See present specification at pg. 19, lines 16-18. However, in the preceding paragraph, the specification indicates that a "toxin-resistant SNARE or toxin-inhibitory SNARE may be a variant, fragment, derivative or fusion of a naturally occurring SNARE with the required or preferred properties as set out above." See present specification at pg. 19, lines 12-14. As such, a toxin-resistant SNARE derived from a variant sequence of a naturally occurring SNARE or a toxin-inhibitory SNARE derived from a variant sequence of a naturally occurring SNARE must possess required or preferred properties as defined by the present specification. For example, one required property a toxin-resistant SNARE or a toxin- inhibitory SNARE is that these SNAREs must in fact be SNAREs. This requirement is self- evident from the plain meaning of the term "SNARE" as used in the present specification and by a person of ordinary skill in the art. As such, the Applicant's respectfully submit that the Examiners interpretation of the term "SNAP-25" to mean any protein, including non- SNARE proteins, is untenable.

B) Second, according to MPEP § 2131, for a reference to anticipated a pending claim, that reference must teach each and every element of the pending claim.

The Carroll patent discloses methods of "treating humans and animals intoxicated with a bacterial toxin by oral administration of antitoxin raised against the toxin." See, col. 3, lines 27-29; and col. 4, lines 21-23. The Carroll patent indicates that a preferred toxin includes BoNT/A, BoNT/B, BoNT/C1, BoNT/D, BoNT/E, BoNT/F, and BoNT/G. See, col. 4, lines 45- 47; and Table 1. The antitoxin antibodies are obtained through immunization of mammals or non-mammals using an antigen. See. col. 4, lines 26-36; and Example s 1 & 3. Thus, the Carroll patent discloses methods of treating poisoning by a clostridial toxin in a patient by administering anti-clostridial toxin antibodies to a patient in need thereof.

Amended Claims 48 and 50 are directed towards a toxin-resistant SNAP-25 or a toxin- inhibitory SNAP-25 "capable of performing substantially the equivalent function to a naturally-occurring SNAP-25." As such, the anti-clostridial neurotoxin antibodies disclosed in the Carroll patent do not anticipate presently claimed methods because anti-clostridial neurotoxin antibodies are incapable of performing substantially the equivalent function to a naturally-occurring SNAP-25

Thus, the Applicants respectfully submit that the Carroll patent does not teach a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 as presently claimed because the anti-clostridial neurotoxin antibodies disclosed in the Carroll patent are 1) not SNAP-25 molecules; and 2) are incapable of performing substantially the equivalent function to a naturally-occurring SNAP-25.

Applicant's arguments have been successfully considered and deemed non-persuasive.

Examiner's Response to Applicant's Arguments:

A) Examiner's disagree with assertion that the meaning for the term "SNAP-25." (see specification pg. 19 lines 15-27).

B) Examiner accepts that the Carroll patent discloses methods of "treating humans and animals intoxicated with a bacterial toxin by oral administration of antitoxin raised against the toxin." See, col. 3, lines 27-29; and col. 4, lines 21-23. The Carroll patent indicates that a preferred toxin includes BoNT/A, BoNT/B, BoNT/C1, BoNT/D,

BoNT/E, BoNT/F, and BoNT/G. See, col. 4, lines 45- 47; and Table 1. The antitoxin antibodies are obtained through immunization of mammals or non-mammals using an antigen. See. col. 4, lines 26-36; and Example s 1 & 3. Thus, the Carroll patent discloses methods of treating poisoning by a clostridial toxin in a patient by administering anti-clostridial toxin antibodies to a patient in need thereof.

Examiner accepts amended Claims 48 and 50 are directed towards a toxin-resistant SNAP-25 or a toxin- inhibitory SNAP-25 "capable of performing substantially the equivalent function to a naturally-occurring SNAP-25."

Examiner disagrees that the anti-clostridial neurotoxin antibodies disclosed in the Carroll patent do not anticipate presently claimed methods because anti-clostridial neurotoxin antibodies are incapable of performing substantially the equivalent function to a naturally-occurring SNAP-25.

Carroll et al teach a method of treating and preventing poisoning by a clostridial toxin in a patient (infant and adult) in need thereof, the method comprising the step of administering an effective amount of a toxin-resistant SNAP-25 (antitoxin) or a toxin-inhibitory SNAP-25 (antitoxin) to the patient and thus this limitation of antitoxin correlates with the teachings of the specification of SNAP-25 (i.e. any protein) (see specification pg. 19 lines 15-27). Carroll et al teach that a toxin-resistant SNAP-25 (antitoxin) inherently is a SNAP-25 toxin-resistant is a SNAP-25 capable of performing substantially the equivalent function to a naturally occurring SNAP-25, but resistant to proteolysis by the clostridial toxin, wherein the toxin-inhibitory SNAP-25 is a SNAP-25 capable of inhibiting the protease activity of the clostridial toxin, wherein administration of the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 produces a clinically useful or significant reduction in a symptom of poisoning caused by the clostridial toxin in the patient suffering from clostridial toxin poisoning, wherein the clostridial toxin is a botulinum toxin type A, wherein the clostridial toxin is botulinum toxin type C1, wherein the clostridial toxin is botulinum toxin type E, wherein the clostridial toxin poisoning is botulism (see abstract, column 3 lines 25-67, column lines 1-10 lines 24-57, column 5 lines 61-67, column 7 lines 9-31 see claims columns 21-22). Therefore, Carroll et al meet the limitation of the instant claims.

As outlined previously, the instant claims are to drawn to a method of treating and preventing poisoning by a clostridial toxin in a patient in need thereof, the method comprising the step of administering an effective amount of a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 to the patient, wherein the toxin-resistant SNAP-25 is a SNAP-25 resistant to proteolysis by the clostridial toxin, wherein the toxin-inhibitory SNAP-25 is a SNAP-25 capable of inhibiting the protease activity of the clostridial toxin, wherein administration of the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 produces a clinically useful or significant reduction in a symptom of poisoning caused by the clostridial toxin in the patient suffering from clostridial toxin poisoning.

Carroll et al teach a method of treating and preventing poisoning by a clostridial toxin in a patient (infant and adult) in need thereof, the method comprising the step of administering an effective amount of a toxin-resistant SNAP-25 (antitoxin) or a toxin-inhibitory SNAP-25 (antitoxin) to the patient and thus this limitation of antitoxin correlates with the teachings of the specification of SNAP-25 (i.e. any protein) (see specification pg. 19 lines 15-27). Carroll et al teach that a toxin-resistant SNAP-25 (antitoxin) inherently is a SNAP-25 resistant to proteolysis by the clostridial toxin, wherein the toxin-inhibitory SNAP-25 is a SNAP-25 capable of inhibiting the protease activity of the clostridial toxin, wherein administration of the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 produces a clinically useful or significant reduction in a symptom of poisoning caused by the clostridial toxin in the patient suffering from clostridial toxin poisoning, wherein the clostridial toxin is a botulinum toxin type A, wherein the clostridial toxin is botulinum toxin type C1, wherein the clostridial toxin is botulinum toxin type E, wherein the clostridial toxin poisoning is botulism (see abstract, column 3 lines 25-67, column lines 1-10 lines 24-57, column 5 lines 61-67, column 7 lines 9-31 see claims columns 21-22).

As to dependent claims 57-61, the method of Carroll et al would inherently teach a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 comprising a replacement of a residue equivalent to residue 197 of full length SNAP-25 by a residue other than Q, a

toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 comprising a replacement of a residue equivalent to residue 198 of full length SNAP-25 by a residue other than R, wherein a residue equivalent to residue Q197 of full length SNAP-25 is replaced, by a residue selected from the group consisting of A, K and W, wherein the residue equivalent to R198 of full length human SNAP-25 is replaced by a residue selected from the group consisting of A, T, K, H and W. Carroll et al would inherently teach a toxin-resistant SNAP-25 capable of performing substantially the equivalent function of a SNAP-25 endogenously present in a patient because SNAP-25 is a variant as described in the specification with insertions, deletions and substitutions and would also inherently be capable of performing substantially the equivalent function of a SNAP-25 in the absence of evidenced to the contrary (see specification pg. 19 lines 15-27).

5. The rejection of claims 48, 53, 57-62 and 69 under 35 U.S.C. 102(b) as being anticipated by anticipated by Roland et al 1986 CMAJ, Vol. 135 pgs. 130-131 is maintained for the reason set forth in the previous office action.

Applicant arguments:

A) The Roland reference discusses the case history of an infant diagnosed with botulism. Initially believing the infant had an infection, health care providers administered the patient ampicillin and gentamicin. See pg. 130, col. 1, I[1, lines 3-7. However, 20 minutes after administering the antibiotics, the infant's condition worsen and assisted ventilation was required. See pg. 130, col. 1, I[1, lines 7-9. Subsequently, examination of stool samples revealed the presence of BoNT/A bacteria and toxin and a diagnosis of infant botulism was made. See pg. 130, col. 2, I[2, lines 1-7. The Roland reference indicated that the infant slowly recovered over two months with supportive treatment. See pg. 130, col. 2, I paragraph 2, lines 7-8.

First, as discussed above, amended Claims 48 and 50 are directed towards a method of treating or preventing poisoning by a Clostridial toxin in a patient in need thereof. The Roland reference does not anticipate the presently claimed methods because ampicillin was administered to treat an infection in a patient in need thereof

and not Clostridial toxin in a patient in need thereof. In fact, the Roland reference indicates that administering the antibiotics worsen the patient's condition when it states"[t]reatment with aminoglycosides for suspected infection, as in our patient, may have worsen the clinical picture." See pg. 130, col. 2, l] 4, line 1 through pg. 131, col. 1, l] 1, line 2. As such, the method of treating an infection disclosed in the Roland reference does not anticipate presently claimed methods because treating a patient with ampicillin neither treats nor prevents poisoning by a Clostridial toxin.

B) The use of ampicillin as disclosed in Roland reference does not anticipate the toxin- resistant SNAP-25 or toxin-inhibitory SNAP-25 presently claimed. Ampicillin is a 13-Lactam antibiotic that functions as a bactericide by inhibiting the synthesis of the peptidoglycan layer of bacterial cell walls. As discussed above, the term SNAP-25 does not mean any protein and amended Claims 48 and 50 are directed towards a toxin-resistant SNAP-25 or a toxin- inhibitory SNAP-25 "capable of performing substantially the equivalent function to a naturally-occurring SNAP-25." As such, ampicillin disclosed in the Roland reference does not anticipate presently claimed methods because ampicillin is incapable of performing substantially the equivalent function to a naturally-occurring SNAP-25.

Thus, the Applicants respectfully submit that the Roland reference does not teach a toxin- resistant SNAP-25 or a toxin-inhibitory SNAP-25 as presently claimed because 1) the Roland reference does not disclose a method to treat or prevent poisoning by a Clostridial toxin and 2) ampicillin is not a SNAP-25 molecule and is incapable of performing substantially the equivalent function to a naturally-occurring SNAP-25.

Applicant's arguments have been successfully considered and deemed non-persuasive.

Examiner's Response to Applicant's Arguments:

A) Examiner accepts that the Roland reference discusses the case history of an infant diagnosed with botulism. Initially believing the infant had an infection, health care providers administered the patient ampicillin and gentamicin. See pg. 130, col. 1, I[1, lines 3-7. However, 20 minutes after administering the antibiotics, the infant's condition worsen and assisted ventilation was required. See pg. 130, col. 1, I[1, lines 7-9. Subsequently, examination of stool samples revealed the presence of BoNT/A bacteria and toxin and a diagnosis of infant botulism was made. See pg. 130, col. 2, I[2, lines 1-7. The Roland reference indicated that the infant slowly recovered over two months with supportive treatment. See pg. 130, col. 2, I paragraph 2, lines 7-8.

Examiner accepts that amended Claims 48 and 50 are directed towards a method of treating or preventing poisoning by a Clostridial toxin in a patient in need thereof. The Roland reference does not anticipate the presently claimed methods because ampicillin was administered to treat an infection in a patient in need thereof and not Clostridial toxin in a patient in need thereof. In fact, the Roland reference indicates that administering the antibiotics worsen the patient's condition when it states"[t]reatment with aminoglycosides for suspected infection, as in our patient, may have worsen the clinical picture." See pg. 130, col. 2, paragraph 4, line 1 through pg. 131, col. 1, paragraph 1, line 2.

Examiner disagrees that the method of treating an infection disclosed in the Roland reference does not anticipate presently claimed methods because treating a patient with ampicillin neither treats nor prevents poisoning by a Clostridial toxin.

Roland et al teach a method of treating poisoning by a clostridial toxin in a patient (infant) in need thereof, the method comprising the step of administering an effective amount of a toxin-resistant SNAP-25 (ampicillin) or a toxin-inhibitory SNAP-25 (ampicillin) to the patient and thus this limitation of ampicillin correlates with the teachings of the specification of SNAP-25 (i.e. any protein) (see specification pg. 19 lines 15-27). Roland et al teach that a toxin-resistant SNAP-25 (ampicillin) inherently is a SNAP-25 resistant to proteolysis by the clostridial toxin, wherein the toxin-inhibitory SNAP-25 (ampicillin) is a SNAP-25 (ampicillin) capable of inhibiting the protease activity of the clostridial toxin, wherein administration of the toxin-resistant SNAP-25 or

the toxin-inhibitory SNAP-25 (ampicillin) produces a clinically useful or significant reduction in a symptom of poisoning caused by the clostridial toxin in the patient suffering from clostridial toxin poisoning, wherein the clostridial toxin is a botulinum toxin type A, wherein the clostridial toxin poisoning is botulism (see Case Report).

B) Examiner disagrees that the use of ampicillin as disclosed in Roland reference does not anticipate the toxin- resistant SNAP-25 or toxin-inhibitory SNAP-25 presently claimed. Examiner disagrees that the term SNAP-25 does not mean any protein. Examiner interprets SNAP-25 to mean any protein thus capable of performing substantially the equivalent function to a naturally occurring SNAP-25 (i.e. any protein). (see specification pg. 19 lines 15-27).

As outlined previously, the instant claims are to drawn to a method of treating and preventing poisoning by a clostridial toxin in a patient in need thereof, the method comprising the step of administering an effective amount of a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 to the patient, wherein the toxin-resistant SNAP-25 is a SNAP-25 resistant to proteolysis by the clostridial toxin, wherein the toxin-inhibitory SNAP-25 is a SNAP-25 capable of inhibiting the protease activity of the clostridial toxin, wherein administration of the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 produces a clinically useful or significant reduction in a symptom of poisoning caused by the clostridial toxin in the patient suffering from clostridial toxin poisoning.

Roland et al teach a method of treating poisoning by a clostridial toxin in a patient (infant) in need thereof, the method comprising the step of administering an effective amount of a toxin-resistant SNAP-25 (ampicillin) or a toxin-inhibitory SNAP-25 (ampicillin) to the patient and thus this limitation of ampicillin correlates with the teachings of the specification of SNAP-25 (i.e. any protein) (see specification pg. 19 lines 15-27). Roland et al teach that a toxin-resistant SNAP-25 (ampicillin) inherently is a SNAP-25 resistant to proteolysis by the clostridial toxin, wherein the toxin-inhibitory SNAP-25 (ampicillin) is a SNAP-25 (ampicillin) capable of inhibiting the protease

activity of the clostridial toxin, wherein administration of the toxin-resistant SNAP-25 or the toxin-inhibitory SNAP-25 (ampicillin) produces a clinically useful or significant reduction in a symptom of poisoning caused by the clostridial toxin in the patient suffering from clostridial toxin poisoning, wherein the clostridial toxin is a botulinum toxin type A, wherein the clostridial toxin poisoning is botulism (see Case Report).

As to dependent claims 57-61, the method of Roland et al would inherently teach a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 comprising a replacement of a residue equivalent to residue 197 of full length SNAP-25 by a residue other than Q, a toxin-resistant SNAP-25 or a toxin-inhibitory SNAP-25 comprising a replacement of a residue equivalent to residue 198 of full length SNAP-25 by a residue other than R, wherein a residue equivalent to residue Q197 of full length SNAP-25 is replaced, by a residue selected from the group consisting of A, K and W, wherein the residue equivalent to R198 of full length human SNAP-25 is replaced by a residue selected from the group consisting of A, T, K, H and W. Carroll et al would inherently teach a toxin-resistant SNAP-25 capable of performing substantially the equivalent function of a SNAP-25 endogenously present in a patient because SNAP-25 is a variant as described in the specification with insertions, deletions and substitutions and would also inherently be capable of performing substantially the equivalent function of a SNAP-25 in the absence of evidenced to the contrary (see specification pg. 19 lines 15-27).

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claim 48 and 50 independent claims, and all dependent claims 53-55, 57-60, 62, 69-70, 73, and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 48 and 50 independent claims, and all dependent claims 53-55, 57-60, 62, 69-70, 73, and 75, the term "substantially" is a relative term, which renders the claims indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Conclusion

Status of the Claims

7. No claims are allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

MARK NAVARRO
PRIMARY EXAMINER